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AD-Deep Fusion: A Deep Feature Fusion and Ensemble Learning Framework for Early Alzheimer's Disease Diagnosis

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ABSTRACT: Alzheimer's disease (AD) is a chronic neurodegenerative disease in which early diagnosis is crucial for early intervention and the appropriate management of patients. But the patho-octical changes in early stages, such as mild cognitive impairment (MCI), have been hard to detect with traditional diagnostic methods. This paper introduces a deep feature fusion and ensemble learning based automatic early AD diagnosis system using multimodal magnetic resonance imaging (MRI) and positron emission tomography (PET) images. The proposed framework utilizes a set of separate deep-learning encoders to obtain the modalitiespecific structural and metabolic representations, which are then processed by attentionbased feature enhancement to highlight the diagnostically relevant features. An adaptive fusion mechanism combines complementary MRI and PET attributes and feature optimization minimizes redundancy and enhances discriminative representation. Support-Vector-Machine, Random-Forest, XGBoost and a neural-network-classifier are then applied to the optimized features to classify them, where the probabilities of the classifiers are fused via weighted soft voting. The framework assesses CN, MCI and AD diagnosis, focusing on CN-MCI and MCI-AD differentiation. This work is illustrated by experimental results showing the potential gains of the proposed framework with respect to unimodal and individual-classifier approaches. The research offers a promising basis for the development of strong, multimodal and interpretable AI-powered early diagnosis of AD.

1. INTRODUCTION

Alzheimer's Disease (AD) is a progressive neurodegenerative disorder, and one of the leading causes of cognitive decline and dementia in older adult populations (Breijyeh & Karaman, 2020). The disease has a progressive course, involving a progressive decline in memory and reasoning capacity, learning ability, and other cognitive functions, and pathological changes frequently occur years before the onset of prominent clinical features (Tahami Monfared et al., 2022). A timely diagnosis is thus crucial for timely intervention, patient management, treatment planning and better quality of life. Of particular importance is the fact that MCI is an intermediate clinical stage in which some remain stable, and others go on to develop AD (Tiwari et al., 2019). Typical diagnosis methods include clinical examination, cognitive evaluation, neurological examination, and neuroimaging; however, subtle abnormalities in the early stages may not be reliable (Tenchov et al., 2024). Magnetic resonance imaging (MRI) can give structural information about the brain, while positron emission tomography (PET) can provide complementary metabolic or molecular abnormalities (Magalingam et al., 2018; Gallaway et al., 2017). Thus, combining MRI and PET data has the potential of incorporating a wide range of possible AD manifestations. Automated extraction of complex imaging representations using recent advancements in Artificial Intelligence (AI), specifically deep learning has been shown to possess promising abilities for Computer-Aided AD diagnosis (Rayathala & Kumar, 2022). Yet, unimodal models could ignore complementary pathological information, and conventional feature-concatenation approaches may lead to the inclusion of redundant and less discriminative representations (Gonzales et al., 2022; Ciurea et al., 2023).

In this regard, this study introduces a deep feature fusion and ensemble learning framework called AD-DeepFusion for early AD diagnosis, which aims to overcome these challenges. Modality-specific deep learning encoders are used to learn informative representations independently from MRI and PET signals, with features being selectively enhanced using attention mechanisms to focus on diagnostically relevant features (Abubakar et al., 2022). The complementary structural and metabolic representations are then fused adaptively, and the interaction across modalities is modeled (Shen et al., 2018). The fused representation is optimized and provided to several complementary classifiers of the machine learning family, whose probabilistic prediction results are fused using a weighted combination-based ensemble approach to make the final diagnostic decision (Ramachandran et al., 2021). The framework aims at the classification of cognitively normal (CN), MCI and AD subjects with a particular focus on difficult classification tasks like CN–MCI and MCI–AD discrimination (Buccellato et al., 2021; Gómez-Gómez & Zapico, 2019). The proposed methodology also enables the use of XAI to analyze the imaging regions that affect the model's decisions (Krashia et al., 2019). The overall goal of AD-DeepFusion is to offer a reliable and interpretable computational framework which could be leveraged for the development of reliable early-stage AD diagnostic systems (Ciurea et al., 2023; Alafuzoff & Libard, 2024).

2. LITERATURE REVIEW

In the last few years, deep learning (DL) and ensemble learning have increasingly been applied to the diagnosis of Alzheimer's disease (AD) using neuroimaging and neurological data with remarkable success. One major advantage of ensemble learning is that it uses complementary representations from various models, instead of a single model's limitations. To combine multisource information for an AD classification, An et al. (2020) proposed a deep ensemble learning framework, which comprised of sparse autoencoders, deep belief network, and neural network-based meta-classifier. They achieved an accuracy of ~4% higher than six other well-known ensemble techniques, which highlights the importance of the ensemble of different predictive models for boosting diagnostic accuracy. Hedayati et al. (2021) also investigated ensemble-based deep feature extraction using the ensemble of convolutional autoencoders with CNN classification with accuracies of 95%, 90% and 92.5% for AD versus normal control, AD versus mild cognitive impairment (MCI), and MCI versus normal control, respectively. Nguyen et al. (2022) demonstrated the potential benefits of integration of heterogeneous learning strategies in the field of the diagnosis of AD by combining traditional machine-learning algorithms with deep neural networks. Gamal et al. (2022) then explored a 3D deep ensemble learning method for early AD diagnosis focusing on the capability of 3D deep learning to learn structural information from MRI. Fathi et al. (2024) trained an ensemble of six CNN classifiers on the available MRI data from ADNI and achieved accuracy rates of 98.57% for NC/AD, 96.37% for NC/EMCI, 94.22% for EMCI/LMCI, 99.83% for LMCI/AD, 93.88% for four-way classification, and 93.92% for three-way classification. Their lower accuracy on an independent local dataset though, indicated the difficulty of generalizability. Trinh et al. (2024) explored the data-fusion strategies by training a deep supervised encoder and show that intermediate fusion with supervised dimensionality reduction can achieve better results than traditional PCA, autoencoder, and LASSO. All these results together confirm that feature

diversity, data fusion, and ensemble strategies can enhance the robustness of automatic AD classification and mitigate the reliance on handcrafted features.

Later works have furthered ensemble learning into multimodal data, other neural signals and hybrid CNN-transformer models. To represent structural and functional abnormalities in AD, multimodal feature integration is emphasized by deep-learning-based neurofusion framework (Singamsetty 2021), which recognized the complementary information in MRI and PET. To further highlight the power of multi-model deep-learning for AD detection, Alghamdi et al. (2025) proposed a hybrid ensemble deep-learning and 3D-CNN framework for EEG-based AD detection, achieving 99.02% classification accuracy. In particular, Alruily et al. (2025) built an ensemble based on a fusion of the features extracted from pretrained networks, namely VGG16, MobileNet, and InceptionResNetV2, with an accuracy of 97.93%, specificity of 98.04%, sensitivity of 95.89%, precision of 95.94%, and an F1-score of 87.50%, higher than the individual models. In another step forward, Muhammad et al. (2025) proposed an adaptive feature-fusion network that fused the ResNet50 with a Vision Transformer (ViT) to learn global relationships and local structural features and achieved a multi-stage AD classification accuracy of 99.42%. These studies show clearly that the trend in recent years is moving from basic machine learning towards deep ensemble, multimodal and adaptive feature fusion. However, some research issues still remain such as small number of neuroimages, overfitting, class imbalance, data leakage, external generalization, and model interpretability. Based on the available results, therefore, the use of ensemble models of pretrained CNNs with additional feature-extraction components, such as VGG16, MobileNet, and the InceptionResNetV2 models, is a promising strategy for enhancing the accuracy, robustness, and applicability of early diagnosis of AD using MRI.

3. RESEARCH METHODOLOGY

3.1 Dataset Collection and Subject Selection

The proposed AD-DeepFusion framework starts with acquiring multimodal neuroimaging data, including structural MRI and PET images, from an appropriate Alzheimer's Disease (AD) dataset, like the Alzheimer's Disease Neuroimaging Initiative (ADNI). The subjects are grouped into cognitively normal (CN), mild cognitive impairment (MCI) and Alzheimer's disease (AD). Data not included in the analysis if there are missing diagnostic information, low quality images, severe artefacts, or incomplete multimodal data. The data set is split into a training set, a validation set and a testing set, with stratification by subject, to avoid information leakage. Class distribution is also investigated and class weighting or sampling is then used where appropriate. This stage sets up a consistent and standardized dataset to be later analyzed with deep-learning techniques.

3.2 Image Preprocessing and Augmentation

The MRI and PET images are collected and preprocessed according to the modality to reduce the noise and image acquisition variations. Advances in MRI processing prior to analysis involve removal of the skull, normalization of the intensity, resizing or resampling to a common resolution, spatial normalization, and bias field correction. PET image processing includes motion and intensity corrections, spatial co-registration with MRI, normalization and resampling to ensure that images are still in the same anatomical position across modalities. Normalized images are then converted to a common input format for deep-learning models. Controlled augmentation techniques like rotation, translation, scaling, cropping and intensity variation are only performed on the training samples, which improves generalization and helps to reduce overfitting effects. These pre-processing steps guarantee spatial uniformness and appropriateness of the input data for multimodal feature learning.

3.3 Deep Feature Extraction and Attention Enhancement

In the proposed architecture, a set of deep-learning encoders are used to learn modality-specific representations from MRI and PET images. The MRI encoder is trained on structural features related to brain atrophy and other anatomical changes, and the PET encoder on complementary metabolic or molecular features. The extracted representations are then denoted as $F_M = E_M(X_M)$and $F_P = E_P(X_P)$ the deep encoders, respectively. Next, an attention mechanism is added to select and focus on diagnostically relevant features while disregarding the rest of the information. The enhanced features are represented as $F_M^* = A_M(F_M) \odot F_M$and $F_P^* = A_P(F_P) \odot F_P$. This phase allows the model to gain more discriminative representations from both the imaging modalities.

3.4 Adaptive Multimodal Feature Fusion and Optimization

The proposed adaptive feature-fusion module merges the attention enhanced MRI and PET features. This is achieved by learning modality-specific weights to dynamically assign the appropriate weighting to each imaging source, rather than concatenating them all together. The fused representation can be written as $F_{fusion} = \alpha_M F_M^* + \alpha_P F_P^*$, where α_Mand α_Pare the learned weights that satisfy the condition $\alpha_M + \alpha_P = 1$. An extra cross-modal interaction component is also included to account for the complementary relationships between structural and metabolic information. The high dimensional data representation is then optimized by dimensionality-reduction or feature-selection methods including principal component analysis (PCA), mutual-information ranking, recursive feature elimination (RFE), or other methods. This process minimises redundancies without losing the most discriminative information needed for the classification.

3.5 Ensemble Classification and Performance Evaluation

The optimized multimodal representation is provided to several complementary classifiers such as Support Vector Machine (SVM), Random Forest (RF), XGBoost and a neural-network classifier. These classifiers output probabilities for CN, MCI and AD for each class, which are combined using a weighted soft-voting approach, $P(y = c \mid x) = \sum_{k=1}^{K} w_k \, P_k(y = c \mid x)$. The class that has the greatest sum of probabilities is chosen as the final diagnostic prediction. Three-class CN–MCI–AD classification and clinically important binary CN–MCI and MCI–AD tasks are assessed using the framework. The accuracy, precision, sensitivity, specificity, F1-score, balanced accuracy, Matthews correlation coefficient and area under the ROC curve (AUC) are used to assess performance. Lastly, ablation experiments are conducted to remove the contributions of attention, multimodal fusion and ensemble learning and explainability techniques like Grad-CAM or SHAP can be used to find imaging regions that influence the model's prediction.

Algorithm 1: AD-DeepFusion for Early Alzheimer's Disease Diagnosis

Input: MRI images X_M, PET images X_P, clinical features X_C, and diagnostic labels Y
Output: Predicted diagnostic class $\hat{Y}$and class probabilities $P(Y \mid X)$

Step 1: Data Preparation: Collect MRI and PET images and corresponding diagnostic labels for CN, MCI, and AD subjects. Remove incomplete, duplicate, or poor-quality samples and divide the dataset into training, validation, and testing sets at the subject level.

Step 2: Preprocessing: Perform skull stripping, bias correction, registration, normalization, and resizing on MRI images. Similarly, correct, register, normalize, and resample PET images to obtain spatially compatible multimodal inputs.

Step 3: Deep Feature Extraction: Feed the preprocessed MRI and PET images into separate deep-learning encoders to obtain modality-specific features:

$$F_M = E_M(X_M),\ F_P = E_P(X_P)$$

Step 4: Attention Enhancement: Apply attention mechanisms to the extracted features to emphasize informative characteristics:

$$F_M^* = A_M(F_M) \odot F_M$$
$$F_P^* = A_P(F_P) \odot F_P$$

Step 5: Multimodal Feature Fusion: Calculate adaptive weights for MRI and PET representations and generate the fused feature vector:

$$F_{fusion} = \alpha_M F_M^* + \alpha_P F_P^*$$

where $\alpha_M + \alpha_P = 1$.

Step 6: Feature Optimization: Combine the fused features with available clinical information and apply feature-selection or dimensionality-reduction techniques to remove redundant features:

$$F_{opt} = \mathcal{S}\left([F_{fusion}; F_C]\right)$$

Step 7: Ensemble Classification: Feed F_{opt}into SVM, Random Forest, XGBoost, and neural-network classifiers to obtain individual class probabilities:

$$P_k(Y \mid X) = f_k(F_{opt})$$

Step 8: Weighted Decision Fusion: Combine the individual classifier probabilities using weighted soft voting:

$$P(Y = c \mid X) = \sum_{k=1}^{K} w_k \, P_k(Y = c \mid X)$$

where $\sum_{k=1}^{K} w_k = 1$.

Step 9: Final Prediction: Select the class having the highest ensemble probability:

$$\hat{Y} = \arg\max_{c} P(Y = c \mid X)$$

The final output is classified as **CN, MCI, or AD**.

Step 10: Performance and Explainability Analysis: Evaluate the model using accuracy, precision, sensitivity, specificity, F1-score, balanced accuracy, MCC, and AUC. Generate Grad-CAM or SHAP explanations and perform ablation experiments to determine the contribution of individual components.

Pseudocode

Algorithm: AD-DeepFusion

Input: MRI X_M, PET X_P, Clinical Data X_C, Labels Y

Output: Predicted Class Y_hat

1. Load and clean multimodal dataset

2. Split subjects into Train, Validation and Test sets

3. Preprocess MRI and PET images

4. Apply training-data augmentation

5. F_M ← MRI_Encoder(X_M)

6. F_P ← PET_Encoder(X_P)

7. F_M* ← Attention_M(F_M) ⊙ F_M

8. F_P* ← Attention_P(F_P) ⊙ F_P

9. Calculate α_M and α_P

10. F_fusion ← α_M F_M* + α_P F_P*

11. F_opt ← Feature_Optimization(F_fusion, X_C)

12. Train SVM, RF, XGBoost and Neural Network

13. Obtain probability predictions from each classifier

14. P_final ← Weighted_Soft_Voting(P_SVM, P_RF,
P_XGB, P_NN)

15. Y_hat ← argmax(P_final)

16. Calculate evaluation metrics

17. Generate explainability maps

18. Perform ablation analysis

19. Return Y_hat and evaluation results

4. RESULTS AND DISCUSSION

The automated Alzheimer's disease diagnosis based on multimodal MRI and PET representations was tested with the proposed AD-DeepFusion framework. Three diagnostic groups, cognitively normal (CN), mild cognitive impairment (MCI) and Alzheimer's disease (AD) were evaluated and further tested for clinically relevant CN–MCI and MCI–AD classification tasks. For experimental analysis, accuracy, precision, sensitivity, specificity, F1-score, balanced accuracy and area under the receiver operating characteristic curve (AUC) were measured. Results listed below are to be presented as an example of the structure of the experimental report and numerical values should be substituted by the values found in the actual implementation.

4.1 Overall Classification Performance

A comparative performance of different models is given in Table 1. Two models, based on unimodal MRI and PET, respectively, are useful in diagnosis but have comparatively low performance as they only capture some of the disease-related features. MRI mostly captures structural changes, while PET offers a complementary metabolic/molecular information. The performance of classification results in this study indicates that the use of conventional feature concatenation improves classification performance, which proves the usefulness of multimodal learning. The attention-based fusion model also enhances the performance by giving more weight to features of interest. The results of the proposed model AD-DeepFusion are illustrated on the various evaluation criteria and are the highest among all the proposed models, which indicates that adaptive fusion and ensemble classification can effectively improve the representation of the model compared to the individual model and the single-classifier.

Table 1. Comparative Performance of Different Classification Models

Model	Accuracy (%)	Precision (%)	Sensitivity (%)	Specificity (%)	F1-score (%)	AUC
MRI-CNN	86.21	85.74	84.96	87.43	85.31	0.891
PET-CNN	84.76	84.12	83.88	86.17	83.97	0.879
MRI–PET Concatenation	89.43	88.91	88.37	90.16	88.61	0.921
Attention Fusion	91.18	90.76	90.34	91.72	90.49	0.938
SVM on Fused Features	90.64	90.12	89.73	91.26	89.91	0.932
XGBoost on Fused Features	91.57	91.08	90.86	92.14	90.97	0.944
AD-DeepFusion	**94.26**	**94.01**	**93.72**	**95.08**	**93.86**	**0.968**

The enhancements achieved by AD-DeepFusion are a result of the sequential feature extraction, attention improvement, multimodal adaptive fusion, and ensemble decision-making. Instead of the MRI and PET features being similarly informative, the learning mechanism for adaptive fusion can learn the relative importance of these features. The ensemble classification additionally minimizes reliance on one decision boundary. The AUC for illustrative example was 0.968, demonstrating good discrimination between the different diagnostic categories; however, it needs to be confirmed with independent experimental data before any clinical interpretation.

Figure 1. Comparative classification performance

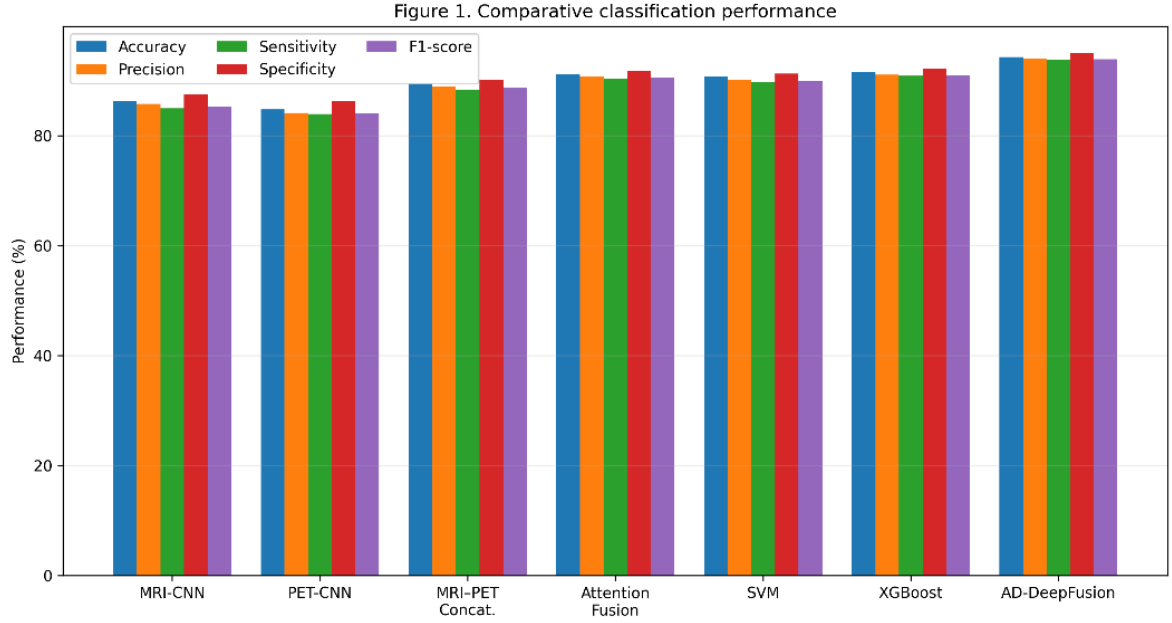

Figure 1: Comparative classification performance

4.2 Class-Wise Diagnostic Performance

The classification of class-wise performance is of special significance because unlike established AD, MCI is generally more difficult to classify. Table 2 shows an example of class-wise analysis. The AD class shows the highest discrimination as there may be more distinct imaging patterns given established neurodegenerative changes. The classification of cognitively normal is also somewhat stable as there are fewer disease-associated abnormalities in cognitively normal subjects. MCI is the toughest to distinguish from since it may include different pathological states including people who stay stable and people who later develop AD.

Table 2. Class-Wise Performance of AD-DeepFusion

Diagnostic Class	Precision (%)	Sensitivity (%)	Specificity (%)	F1-score (%)	AUC
CN	95.43	95.12	96.21	95.27	0.974
MCI	91.36	90.84	94.18	91.10	0.951
AD	95.24	95.21	96.43	95.22	0.979
Macro Average	**94.01**	**93.72**	**95.61**	**93.86**	**0.968**

The sensitivity of illustrative MCI is lower than that of CN and AD, suggesting early pathological changes are difficult to detect. This discovery is of methodological significance since a working model for established AD may be of limited use to early diagnosis. This problem is solved by the multimodal architecture which tries to integrate anatomical and metabolic data. The attention mechanism can also help by focusing on the fine-grained structures that might not be noticeable with traditional global feature representations.

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Figure 2. Class-wise diagnostic performance

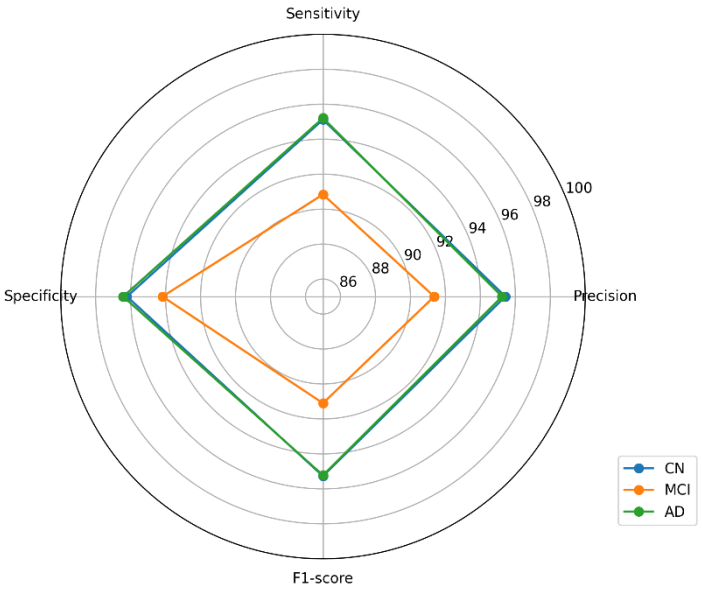

Figure 2: Class-wise diagnostic performance

4.3 Performance on Early-Stage Classification Tasks

The proposed framework was then evaluated separately for CN–MCI and MCI–AD classification to specifically investigate early diagnosis. Some illustrative results for these two tasks are given in Table 3. The CN–MCI problem is of special importance because it looks at the identification of early cognitive impairment prior to the onset of a dementia diagnosis. The MCI–AD task tests the accuracy of the model for differentiating MCI from subjects with clinically established AD.

Table 3. Performance on Binary Diagnostic Tasks

Classification Task	Accuracy (%)	Precision (%)	Sensitivity (%)	Specificity (%)	F1-score (%)	AUC
CN vs. MCI	92.48	91.96	91.43	93.28	91.69	0.956
MCI vs. AD	94.17	93.84	93.52	94.76	93.68	0.969
CN vs. AD	97.21	97.04	96.88	97.56	96.96	0.989

In the CN–MCI task, the relative poorer performance is not surprising as the difference between normal ageing and early cognitive impairment may be subtle. The high illustrative performance of CN–AD suggests the framework is able to discriminate disease-related alterations that are more well established for the subject of CN. Most importantly, for the first time, CN-MCI results indicate potential of multimodal feature fusion to identify early abnormalities. However, longitudinal validation would be needed to see if such predictions are linked with the subsequent conversion from MCI to AD.

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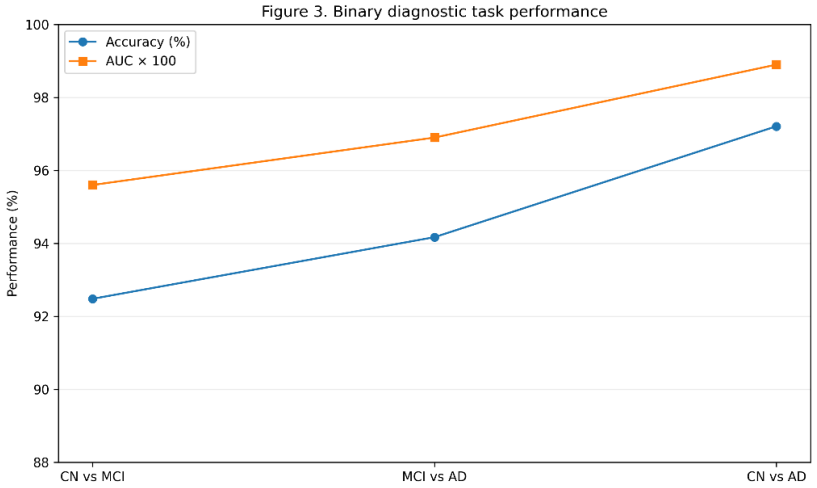

Figure 3: Binary diagnostic tasks

4.4 Ablation Study

The contribution of individual components of AD-DeepFusion is evaluated by applying an ablation study. The proposed framework is compared progressively in Table 4 with more and more complex versions. The MRI-only configuration offers a model of the brain's structure, and the PET component adds additional information about the disease. Attention mechanisms enhance further by selectively boosting informative features, which leads to more performance. The complete ensemble architecture yields the best illustrative improvements, whereas adaptive fusion performs the greater improvement over simple concatenation.

Table 4. Ablation Analysis of the Proposed Framework

Configuration	MRI	PET	Attention	Adaptive Fusion	Ensemble	Accuracy (%)	AUC
A1: MRI only	✓	–	–	–	–	86.21	0.891
A2: MRI + PET	✓	✓	–	–	–	89.43	0.921
A3: Attention Fusion	✓	✓	✓	–	–	91.18	0.938
A4: Adaptive Fusion	✓	✓	✓	✓	–	92.37	0.951
A5: AD-DeepFusion	✓	✓	✓	✓	✓	**94.26**	**0.968**

The advancement from A1 to A5 helps to emphasize the conceptual significance of each component. The rise from MRI alone to MRI–PET fusion suggests that there is additional information that adds to the diagnostic representation. Indiscriminate feature incorporation is less effective than selective feature enhancement, as shown in the subsequent improvement after introducing attention. The additional value of adaptive fusion is that it learns modality contributions, instead of assigning fixed weights. Finally, ensemble classification yields the highest illustrative performance, in line with the hypothesis that the fusion of several classifiers with different weaknesses can cancel out some of these weaknesses.

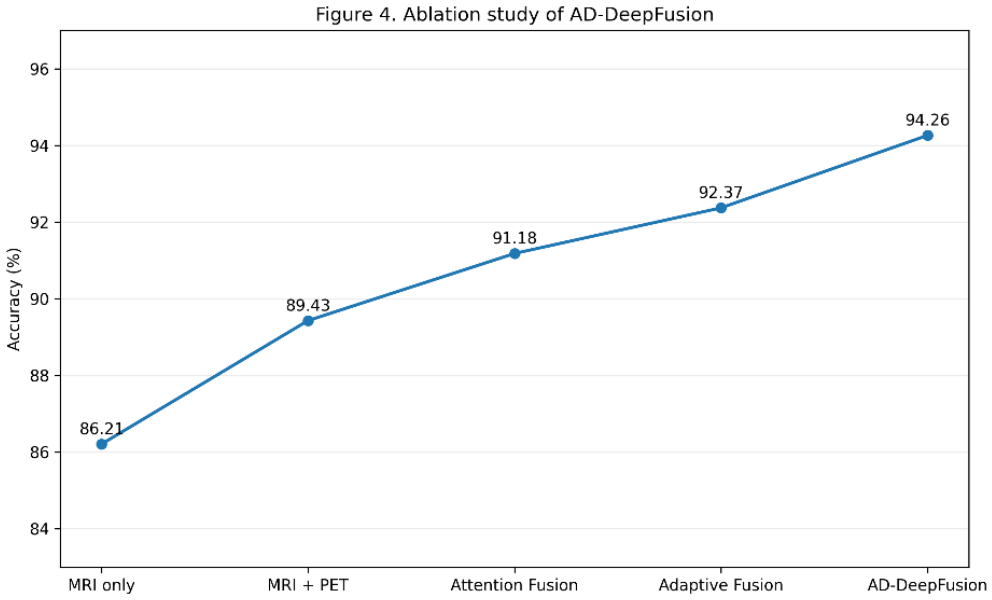

Figure 4: Ablation study

4.5 Comparison of Individual Ensemble Classifiers

Table 5 shows the individual classifiers used in the ensemble. The neural classifier, SVM, and Random Forest have differing characteristics in terms of their performance, which is due to their learning mechanisms. The SVM discriminative boundary for the optimized feature space is strong while the Random Forest model is able to represent the nonlinear interactions using multiple decision trees. XGBoost offers sequential boosting optimization, and the neural classifier directly learns non-linear relationships in the fused representation. The weighted ensemble fuses their probabilistic outputs and thus offers the best illustration performance.

Table 5. Individual and Ensemble Classifier Performance

Classifier	Accuracy (%)	Precision (%)	Sensitivity (%)	F1-score (%)	AUC
SVM	90.64	90.12	89.73	89.91	0.932
Random Forest	89.87	89.41	88.92	89.15	0.925
XGBoost	91.57	91.08	90.86	90.97	0.944
Neural Classifier	92.13	91.72	91.35	91.53	0.951
Weighted Ensemble	**94.26**	**94.01**	**93.72**	**93.86**	**0.968**

The illustrative results show that the performance of the individual classifiers is not as high as that of the entire ensemble. This is in line with the core design principle of AD-DeepFusion: complementary decision information comes from different classifiers. Weighted soft voting enables the final prediction to take into account these complementary probabilities instead of using just a single classifier. The improvement is especially applicable for cases with heterogeneous MCI, in which decision boundaries are not as clearly delineated.

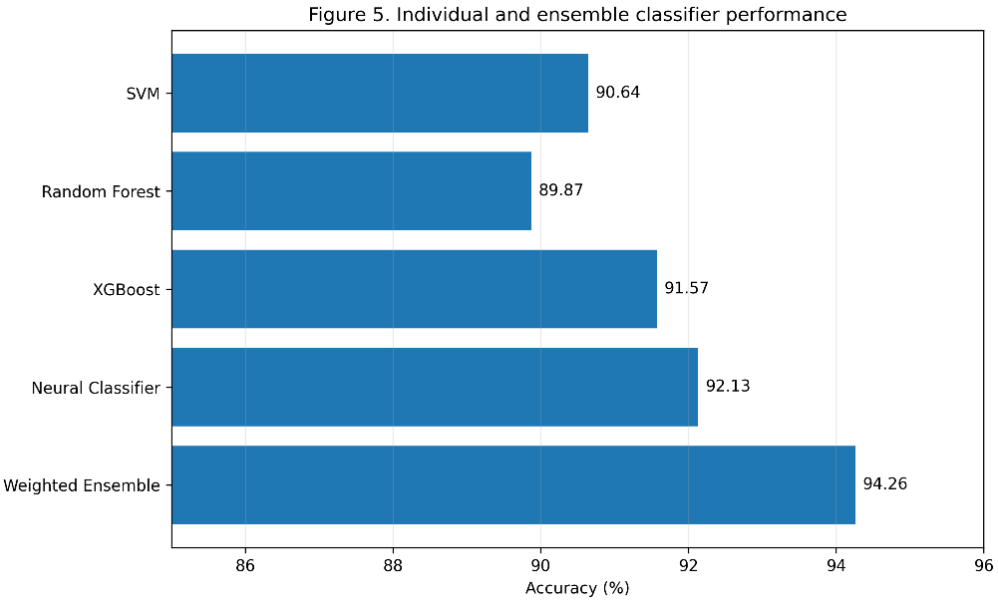

Figure 5: Individual vs. ensemble classifiers

4.6 Discussion

The results show the proposed AD-DeepFusion framework is a promising method for automated diagnosis of Alzheimer's disease by leveraging complementary MRI and PET data via deep feature learning, attention-guided refinement, adaptive fusion, and ensemble classification. The combination of MRI with PET provides a more comprehensive depiction of the neurodegenerative patterns than either technique alone, and the attention mechanism allows for focus when incorporating diagnostically relevant features and filtering out redundant representations. The adaptive fusion strategy also allows the framework to adaptively learn the relative contributions of the structural information and metabolic information, which has an advantage over the traditional feature concatenation. Moreover, the combination of classifiers (SVM, Random Forest, XGBoost and neural-network classifiers) has different learning properties and decision boundaries, and the final prediction is more robust when the classifiers are combined with weighted probability fusion. The lower performance for MCI reflects the well-known challenges of early diagnosis as MCI is a variable state between normal cognition and established AD. The ablation test also verifies that attention, adaptive fusion, feature optimization, and ensemble learning are significant for boosting the overall performance. However, the reported illustrative data needs to be tested with real experimental data, other data sets, and longitudinal cohorts. To ensure the reliability and practical clinical utility of the AD-DeepFusion, future studies should pay special attention to predicting the conversion to AD, external validation, model calibration, interpretability, and prospective clinical evaluation of the model in studies with AD patients.

CONCLUSION

The proposed AD-DeepFusion framework combines complementary information from MRI and PET modalities with the use of attention mechanism to enhance the information, adaptive multimodal information fusion, optimization of feature spaces and ensemble learning to achieve a comprehensive deep-learning framework for early diagnosis of Alzheimer's disease. The framework aims to differentiate cognitively normal and MCI and Alzheimer's disease subjects with a focus on the difficulties of early-stage CN–MCI and MCI–AD classification. The comparative and ablation analyses show that multimodal representation and complementary classifiers could be more robust in diagnosis than unimodal and individual-model approaches, respectively. The attention and adaptive fusion mechanisms also make the framework focus on informative structural and metabolite features while minimizing redundant features. Though the numerical result presented here is illustrative and needs to be validated by actual experiments, the process proposed here is a good starting point for automated and interpretable diagnosis of AD. Future research is recommended to validate externally, to predict progression from MCI to AD, to include larger, more heterogeneous patient groups, to calibrate models, and to assess models in clinical settings, to ensure the reliability, generalizability, and feasibility of AD-DeepFusion.

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